REMARKS/ARGUMENTS

Claims 21, 23-27, 31-34, 38-41, 45-48, and 52 are pending. No claims have been added, amended, or canceled. The amendment submitted herein adds a claim of priority to application Serial No. 08/108,591 and international application PCT/EP92/01219.

As a preliminary matter, the finality of the present Office Action is premature because it introduces a new rejection that was not necessitated by any claim amendment. The Office Action dated January 15, 2003, withdraws rejections and/or objections not reinterated from prior office actions (January 15, 2003, Office Action, page 2). Significantly, the January 15 Office Action does not include any rejection under 35 U.S.C. §§ 102 or 103. Although Applicants responded to the January 15 Office Action on April 2, 2003, they did not amend any of the pending claims. Nonetheless, the instant Office Action presents rejections under 35 U.S.C. §§ 102 and 103. Because these rejections are not based on any claim amendment, the finality of the instant Office Action is premature and should be withdrawn.

Claims 23, 25-27, and 31 stand rejected as allegedly anticipated by PCT Patent Application WO 92/20702 ("the 702 Application). Claims 23, 25-27, and 31 stand rejected under 35 U.S.C. § 103 as allegedly being obvious in view of the combined teaching of the 702 Application and Renneisen, *et al, Journal of Biological Chemistry*, **1990**, 265, 16337-16342. The basis for these rejections appears to that the 702 Application allegedly "states that k+m is preferably 1 or 2" (Office Action, page 5). The Office Action, however, does not provide any guidance as to where in the 702 Application this statement appears, and Applicants have not been able to locate it. Thus, the rejections are believed to lack evidentiary support. Nonetheless, in an attempt to advance prosecution, Applicants have amended their claim of priority consistent with the Examiner's suggestion (Office Action,

page 3). In view of this amendment, the rejections under §§ 102 and 103 are believed to be moot.

Claims 39-41, 45-48, and 52 stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Applicants respectfully request reconsideration of this rejection, as there is no evidence of record indicating that those skilled in the art would be unable to practice the methods ***as they are claimed.***

Enablement may be provided by "illustrative examples," *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993), and the initial burden is on the PTO to demonstrate an objective factual basis for questioning Applicants' disclosure. *Id.* However, the inquiry cannot stray from the metes and bounds of the claim language itself. *Ex parte Erlich*, 3 U.S.P.Q.2d 1011 (Pat. Off. Bd. App. 1987) (the invention that must be enabled is that defined by the claims).

As best understood, the Office Action alleges that the instant claims are not enabled because it is not known how much therapeutic benefit a particular compound will provide when introduced into an animal. This is evidenced by the following allegation contained in the Final Rejection:

> As discussed in previous Office actions, the present invention is complex, and therapeutic applications using compounds analogous to those claimed here are undeveloped.

(Final Rejection, page 7).

However, this allegation (as well as the others related to cell penetration, target folding, immune system response to foreign matter, and binding of oligonucleotides to blood proteins) falls far short of demonstrating that the compounds recited in the claims would not be expected to exhibit at least some level of activity. Indeed, Applicants do not claim a particular level of activity. Rather, their claims are directed to methods for simply

modulating gene expression. Nothing in the Final Rejection indicates that the claimed compounds will not modulate gene expression to at least some extent.

Significantly, the outstanding Office Action does not appear to assert that those skilled in the art would need to engage in undue experimentation to administer one of the claimed compounds to an organism. Nor does the Final Rejection appear to assert that the claimed compounds will not have some level of activity. Instead, the rejection appears to be resurrecting a stringent requirement of **therapeutic** utility that was unambiguously rejected by the PTO many years ago, see M.P.E.P. § 2107.02; *In re Sichert*, 566 F.2d 1154 (C.C.P.A. 1977) (holding that it is improper for the PTO to require any showing regarding the degree of effectiveness of therapeutic inventions). Enablement requires only that the application teach how to make and use the invention without undue experimentation. *See In re Sichert,* 566 F.2d 1154 (C.C.P.A. 1977). There is no reason to believe that one skilled in the art would be required to perform any amount of undue experimentation to administer the claimed compounds to a subject and achieve some measurable effect.

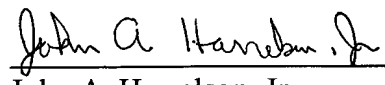
When Applicants' specification is reviewed for support for claimed methods that involve methods for modulating gene expression in an animal by administering certain compounds to an animal, one finds more than ample illustrative examples to meet the enablement standard of *In re Wright, supra.* The specification describes administration and dosing of the instantly claimed compounds at, for example, page 15 line 32 through page 18 line 20.

In view of the foregoing, Applicants submit that the pending claims are fully enabled, and request withdrawal of the rejection under 35 U.S.C. § 112.

Applicants respectfully submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are earnestly solicited.

Respectfully submitted,

Date: August 28, 2003



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